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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/501,295	07/12/2004	Ferdinando Giordano	26177	8153

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EXAMINER	
MAIER, LEIGH C	
ART UNIT	PAPER NUMBER
1623	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/22/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/501,295	GIORDANO ET AL.	
	Examiner	Art Unit	
	Leigh C. Maier	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8 and 10-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 10-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/21/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-8, 10-13 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the free base of pantoprazole (including either or both of the enantiomers), their anhydrous salts, the sodium sesquihydrate and the magnesium dihydrate, does not reasonably provide enablement for the full scope of hydrates and solvates claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Circ. 1988) as follows:

(1) The quantity of experimentation necessary (time and expense);
(2) The amount of direction or guidance presented;
(3) The presence or absence of working examples of the invention;
(4) The nature of the invention;
(5) The state of the prior art;
(6) The relative skill of those in the art;
(7) The predictability or unpredictability of the art; and
(8) The breadth of the claims.

The claims are drawn to all theoretical solvates and hydrates of pantoprazole that might be prepared. However, it appears that only the sodium mono and sesquihydrates, and the magnesium dihydrate are known. See Kohl (WO 00/10995) at page 2, 1st paragraph. There do

not appear to be any known isolated solvates. It is not clear how broad the claims are because it is not possible to predict the number of hydrates and/or solvates that might be prepared. Vippagunta et al (Adv. Drug Deliv. Rev., 2001) addresses the state of the art with respect to the preparation of these types of formulations. See section 3. "The mere presence of water in a system is not a sufficient reason to expect hydrate formation, because some compounds, though they are soluble in water, do not form hydrates." Section 3.1. It is known that pantoprazole forms hydrates, but it is not known how many or what type it is *possible* to form. The specification gives provides not guidance with respect to the preparation of any hydrates not already disclosed in the art. With respect to solvate preparation, the guidance in the specification amounts to speculation that "[i]f pantoprazole is isolated in crystalline form, it may contain variable amounts of solvent." This, of course, is a truism in any crystal formation, but it gives no guidance as to what, if any, solvates *are* or *can be* formed. Per Vippagunta, the mere prediction of what solvates and/or hydrates might be formed is complex and difficult—never mind the actual preparation of said solvates and/or hydrates. In view of the foregoing, one of ordinary skill would require undue experimentation to make and use the inventive product commensurate with the scope of the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4-8, 10, 12, 13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ishiguro et al (WO 96/38175).

Ishiguro teaches the preparation of cyclodextrin inclusion complexes of benzimidazole derivatives and their physiologically acceptable salts. One of the suggested species is pantoprazole. See pages 3 and 22-26. The reference further teaches the further addition of pharmaceutical auxiliaries. See pp. 27-28. Example 3 exemplifies the use of ethanol as the solvent for the preparation of inclusion complexes. The reference further teaches the use of inclusion complexes for the treatment of a number of gastrointestinal disorders. See paragraph bridging pp. 29-30. Regarding claim 7, the reference does not describe the type of inclusion complex that is formed, but inclusion formation is a function of the structure of the guest molecule and the cyclodextrin used, so preparing a pantoprazole:cyclodextrin complex according to Ishiguro would be expected to result in a 1:1 inclusion complex, as recited in the claims. The typical inclusion complex is a 1:1 complex. Ishiguro does not exemplify a pantoprazole:cyclodextrin complex. Only lansoprazole is exemplified.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare a pantoprazole:cyclodextrin complex by substituting pantoprazole for lansoprazole in any of the examples disclosed by Ishiguro. One of ordinary skill would have been motivated to prepare such a complex because it is expressly suggested in the reference. In the absence of unexpected results, the artisan would have a reasonable expectation of success in preparing such a product. It would be further obvious to administer such inclusion complexes in the prevention/treatment protocols expressly suggested in the reference. One of ordinary skill would reasonably expect success in providing such treatment.

Claims 1, 2, 4-8, 10 and 12-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ishiguro et al (WO 96/38175) in view of Kohl (WO 00/10995).

Ishiguro teaches as set forth above. The reference does not teach the use of pantoprazole sodium sesquihydrate or pantoprazole magnesium dihydrate.

Kohl teaches that several salt hydrates of pantoprazole, including pantoprazole sodium sesquihydrate or pantoprazole magnesium dihydrate, are known. See page 2, first paragraph.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to use any known salt form of the benzimidazole species, such as pantoprazole, for the preparation of cyclodextrin inclusion complexes with a reasonable expectation of success for their art-disclosed utility. The artisan would be motivated to use pantoprazole sodium sesquihydrate or pantoprazole magnesium dihydrate because Ishiguro had suggested the use of benzimidazole salts, and Kohl and taught their availability.

Claims 1, 3, 4, 6-8, 12, 13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klokkers et al (WO 98/40069).

Klokkers teaches the preparation of cyclodextrin (including β–cyclodextrin) inclusion complexes of benzimidazole derivatives. One of the suggested species is pantoprazole. See abstract and page 5, first three full paragraphs. See also examples for preparation method. The reference further teaches the further addition of pharmaceutical auxiliaries. See pp. 6-8. Regarding claim 7, complexation formation is addressed above. Klokkers does not exemplify a pantoprazole:cyclodextrin complex. Only omeprazole is exemplified.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare a pantoprazole:cyclodextrin complex by substituting pantoprazole for omeprazole in any of the examples disclosed by Klokkers. One of ordinary skill would have been motivated to prepare such a complex because it is expressly suggested in the reference. In the absence of unexpected results, the artisan would have a reasonable expectation of success in preparing such a product.

Claims 1-4, 6-8, 10, and 12-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Min et al (WO 93/13138) in view of Ishiguro et al (WO 96/38175) and Kohl (WO 00/10995).

Min teaches the preparation of cyclodextrin (including β–cyclodextrin) inclusion complexes of benzimidazole derivatives and salts thereof. The genus of derivatives defined by Formula (I) includes omeprazole and lansoprazole. The reference further teaches the further addition of pharmaceutical auxiliaries. See pp. 4-5. Regarding claim 7, complexation formation is addressed above. The complexes have excellent storage stability, dissolution and absorption properties after oral administration. Min does not teach the use of pantoprazole.

Ishiguro teaches as set forth above. This reference establishes the equivalence among benzimidazole derivatives, such as omeprazole, lansoprazole and pantoprazole, with respect to inclusion complex formation with cyclodextrins.

Kohl teaches as set forth above.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare a cyclodextrin inclusion complex comprising any available salt of

a benzimidazole derivative for the art-disclosed advantages of enhanced dissolution, etc. One of ordinary skill would reasonably expect success in using a pantoprazole salt because Ishiguro had established equivalence between pantoprazole and the benzimidazole derivatives suggested by Min. In the absence of unexpected results, one of ordinary skill would reasonably expect success in using any of the known pantoprazole derivatives, such as those disclosed by Kohl. It would be further obvious to administer these complexes in the prevention/treatment protocols expressly suggested in the reference. One of ordinary skill would reasonably expect success in providing such treatment.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (571) 272-0656. The examiner can normally be reached on Tuesday, Thursday, and Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Anna Jiang (571) 272-0627, may be contacted. The fax number for Group 1600, Art Unit 1623 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished application is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

Leigh C. Maier

Leigh C. Maier
Primary Examiner
December 14, 2006